



INTERNATIONAL INSTITUTE OF SYNTHETIC RUBBER PRODUCERS, INC.

8EHQ-0304-15405

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March 30, 2004



Document Processing Center (Mail Code 7407M)
Room 6428
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1201 Constitution Ave., NW
Washington, DC 20460

CONTAINS NO CBI

Dear 8(e) Coordinator:



8EHQ-03-15405

On behalf of the Chloroprene Scientific Oversight Committee, I wish to inform you of the results from a recently completed Combined Male and Female Fertility and Early Embryonic Developmental Study in male and female rats with the above referenced test substance (2,3-Dichloro-1,3-butadiene). Groups of Crl:CD®(SD)IGS BR rats (24/sex/level) were exposed by inhalation (whole body) to the test substance at mean vapor concentrations of 0, 1, 5 or 50 ppm. Rats were exposed six hours per day during premating (8 weeks), cohabitation of mating pairs (up to 2 weeks), and conception to implantation (1 week).

During the in-life portion of the study, body weight, food consumption, and clinical observation data were collected. Estrous cyclicity was evaluated for 3 weeks prior to cohabitation, and during the cohabitation period. All animals were subjected to a gross pathology examination, on day 21 of gestation for females and at the end of the exposure period for males. The uterus of each pregnant rat was removed and dissected to permit examination of the uterine contents. The fetuses were removed, individually identified, weighed, sexed, and examined for external alterations. Selected organs, including reproductive organs, were weighed (all animals) and examined microscopically (10/sex/group). Sperm motility, morphology, and sperm concentration in testis and epididymis, were evaluated.

No deaths occurred during the exposures. There were reductions in body weight gain and food consumption at 50 ppm in both males and females. Reductions in body weight gain and food consumption observed in 5 ppm males were not considered adverse since these changes were small, transient, and did not affect overall weight gain or food consumption. There were no effects on reproductive parameters (mating, fertility, number of corpora lutea or implants, fetal viability or body weight, pre or post-implantation loss, estrous cycle length, precoital interval, and sperm motility, morphology, and concentration).

Relative to controls, reproductive parameters were unaffected at all exposure concentrations.

Test substance-related histopathological changes were found but occurred only in the nose and only in male and female rats exposed to 50 ppm. In affected males (24/24), olfactory lesions consisted of a depleted sensory cell layer, enlargement of basal cells within the single-cell basal layer, and moderate atrophy of Bowman's glands; the sustentacular cell layer and nerve bundles were normal. The presence of degenerate and necrotic sensory cells within the depleted sensory cell layer and enlarged basal cells suggests that olfactory cell degeneration/regeneration was ongoing and may have reached an equilibrium state. Areas of olfactory mucosal hypercellularity were infrequently observed. In males, olfactory degeneration/regeneration was generally graded as mild.

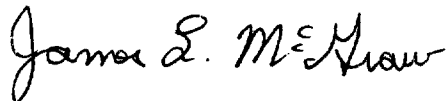
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In affected females (24/24), the olfactory changes were less severe than in males. Unlike males, depletion of the sensory cell layer was uncommon. Sustentacular cells were normal except for degenerative changes noted in scattered areas of hypercellular regeneration. In some areas, olfactory epithelial cysts were formed due to both dilatation of the ducts of Bowman's glands and involution of sustentacular cells as a result of underlying sensory cell loss. These cysts were much more common in females than in males.

Sincerely,

A handwritten signature in cursive script that reads "James L. McGraw".

James L. McGraw
Managing Director & CEO
International Institute of Synthetic Rubber Producers, Inc.

Cc: Rudolf Valentine- Dupont
Mike Kaplan-Dupont